EXPERIMENTS

UPON

THE HEART OF THE DOG

WITH REFERENCE TO THE

MAXIMUM VOLUME OF BLOOD SENT OUT BY THE LEFT VENTRICLE IN A SINGLE BEAT,

AND THE

INFLUENCE OF VARIATIONS IN VENOUS PRESSURE, ARTERIAL PRESSURE, AND PULSE-RATE UPON THE WORK DONE BY THE HEART.

BY

WM. H. HOWELL, A.B.,
FELLOW OF THE JOHNS HOPKINS UNIVERSITY, BALTIMORE,

AND

F. DONALDSON, JUN., A.B.

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VI. *Experiments upon the Heart of the Dog with reference to the Maximum Volume of Blood sent out by the Left Ventricle in a Single Beat, and the Influence of Variations in Venous Pressure, Arterial Pressure, and Pulse-Rate upon the work done by the Heart.*

By WM. H. HOWELL, *A.B., Fellow of the Johns Hopkins University, Baltimore,* *and* F. DONALDSON, Jun., *A.B.*

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[PLATE 7.]

THE most important factor to be determined before calculating the work done by the heart is the quantity of blood forced from the ventricles at each systole. Most of the efforts to determine this quantity have been based either upon faulty observations upon the dead heart, or upon the uncertain data obtained by estimating the mean velocity of the stream of blood in the aorta. Professor MARTIN accordingly suggested to us that we should attempt to measure it directly on the isolated Dog's heart. The work thus undertaken was carried on during the greater part of the university session, 1881-82, and the results obtained are given in the following pages. The method of isolating the heart was essentially that described in Professor MARTIN'S paper (Phil. Trans., 1883, p. 663).

In the course of this work many unexpected difficulties arose, necessitating changes in the apparatus and the method of operating, and preventing us for a long time from obtaining any successful results. In our experiments it was necessary not only that the heart should live and beat, but that it should be in the best possible physiological condition, and any marked pulmonary œdema made an experiment nearly valueless. This most frequent cause of failure was mainly owing to the fact that, on account of the large quantity of blood required for an experiment, we were obliged to use Calf's blood obtained from the butcher; very often this blood, as Professor MARTIN states in his paper, will bring about œdema of the lungs in a short time; large quantities of exuded serum pour out of the tracheal cannula, the air-passages in the lungs become choked up with liquid, and the circulation from the right to the left side of the heart is greatly impeded. We have succeeded, however, in making a considerable number of experiments in which all the conditions

were favourable, the œdema of the lungs not occurring to any marked extent until after many observations had been made.

In speaking briefly of former attempts to compute the amount of blood thrown out from the left ventricle at each systole, it is hardly necessary to refer to the earlier observations made upon dead hearts, since these are universally allowed to be of but little value. We need only say a few words about the later experiments upon living animals made by VOLKMANN, VIERORDT, and FICK.

The method used by VOLKMANN (1) is too well known to require any extended description. It is based upon the principle that the velocity of the blood stream is inversely as the width of the channel in which it flows. The line of argument used is this—starting from the aorta at its origin, which he calls the first vascular section, we have, first, a division into the innominate and the aorta beyond the innominate; this he calls the second vascular section, and supposes that the velocity of the stream in each of the two divisions of this section is the same, and is as much less than the velocity in the undivided aorta as their united sectional areas are greater than the sectional area of the aorta. The innominate in turn divides into branches making a third vascular section; the velocity in each of these branches is again the same, and as much less than the velocity in the innominate as the sum of their sectional areas is greater than the sectional area of the innominate. Then by determining the velocity of the blood in one of these last divisions by means of his hämodromometer, and measuring the width of the different vascular sections mentioned, the necessary data were obtained for estimating the quantity of blood passing through the sectional area of the ascending limb of the aortic arch in a given time, and therefore, knowing the pulse-rate, the quantity of blood sent out from the ventricle at each systole.

The whole method is evidently subject to many serious errors, the most important of which is that the velocity of the blood stream, as has been shown by DOGIEL, undergoes such great variations that but little positive value can be attached to an experimental determination of it at any one time, or even to the mean deduced from many observations.

Besides this, the method employed to determine the width of the vascular sections is open to objection. The means used for determining this factor were briefly these. After obtaining the velocity in the carotid, the diameter of that vessel was measured; the animal then killed, and the vascular system injected from the abdominal aorta with melted wax, and under such a pressure that the carotid assumed the same diameter as that which it had previously when the velocity in it was measured. After the wax had hardened the diameter of the aorta and of the other vessels was obtained. As VOLKMANN himself says, one is not at all sure in this case that the parts of the vascular system under consideration will be distended in the same proportion to each other that existed during life; he thinks, however, that this will make no difference as long as the carotid possesses the same diameter that it had when the velocity in it was measured, since any over-valuation of the width of

the aorta will be balanced by a proportional under-valuation of the velocity in it, and inversely. While this may be true of the aorta as compared with the carotid alone, it will hardly hold with regard to the intervening vessels, the second branch of the third vascular section for instance, any mistake in the diameter of which will introduce an error into the calculation. VIERORDT'S method (2) is based, like that of VOLKMANN, upon the proposition that the mean velocity in the arterial system is inversely as its sectional area. He determined the mean velocity in the carotid by means of his hæmotachometer, obtaining results for the Dog which agree very closely with those obtained by VOLKMANN. Knowing the velocity in the carotid, and accepting the measurements given by KRAUSE for Man of the diameter of the carotid, the sub-clavian, the innominate, and the aorta beyond the point at which the innominate is given off, he deduced the quantity of blood flowing through the sectional area of each of these arterial trunks in a second. The quantity of blood flowing per second through the sectional area of the ascending limb of the aortic arch was taken as equal to the sum of these quantities plus 4 cub. centims. allowed for the coronaries. Knowing the number of systoles occurring in a second, the quantity thrown out at each systole is easily obtained. VIERORDT does not accept the supposition of VOLKMANN that the velocity in each branch of any one vascular section is the same, but thinks it safer to assume that the mean velocity in the aorta beyond the giving off of the innominate is one-fourth greater than that in the innominate. For the ratio of the weight of blood thrown out from the left ventricle at each systole to the body weight, he gets a fraction almost identical with that of VOLKMANN : about $\frac{1}{400}$th.

FICK, in consequence of the unreliable data upon which the results obtained by VOLKMANN and VIERORDT are based, can see in their close agreement only accident. His own method (3) while possessing the advantage, as far as Man is concerned, of being applicable directly to the human subject, rests, however, upon assumptions which cannot be freely allowed. The arm in his method was placed in a sort of plethysmograph, by means of which changes in volume occurring at each systole were registered upon a revolving drum ; from this curve of volume he constructed a curve showing the changes in the strength of the stream in the axillary artery as compared with the strength of the stream in the axillary vein, which was taken as a constant. From a comparison of this curve with the curve of changes of velocity in the carotid of the Horse obtained by CHAVEAU, he endeavoured to give absolute values to the ordinates of his curve, and in this way determined the quantity of blood flowing through the sectional area of the axillary artery in a second ; to obtain the quantity flowing through the sectional area of the sub-clavian in a second he multiplied by two. Then taking the ratio of the strength of stream in the sub-clavian to that in the aorta as given by VIERORDT, he obtained the quantity of blood flowing through the sectional area of the aorta in a second, from which, knowing the pulse-rate, the quantity of blood thrown out at each systole was deduced. The mean of his two experiments

gave about $\frac{1}{1000}$ as the ratio of the weight of blood thrown out at each systole to the body weight.

Before passing on to a discussion of the results of our work it will be necessary to give a brief description of the manner in which observations were made. The apparatus and the method of operation were the same as those described by Professor MARTIN (Phil. Trans., 1883, p. 663). Our Dogs, however, were always anæsthetized by means of a mixture of chloroform and ether, and great care was taken to introduce into the aorta a cannula with as large a bore as possible.

As quickly as possible after the Dog was in the warm chamber, all the connexions made and the heart going well, observations were begun in order to complete a series before pulmonary œdema commenced to impede the flow of blood from the right to the left side of the heart. The chief point in an observation was to determine the quantity of blood pumped out from the left ventricle in thirty seconds. In order to accomplish this, one of us took charge of the kymograph, upon the roll of paper of which was made to write on the same vertical line the pens of two manometers (one recording mean pressure, the other the pulse rate), and of the chronograph, and a marking pen to indicate the period during which the blood was collected from the outflow tube. This person, when an observation was to be made, after allowing the kymograph to run for a few seconds in order to see that the pens were all writing properly, counted aloud 30 seconds, pushing down the handle of the marking pen at the beginning of that time and holding it in that position until the 30 seconds had been counted. The other person meanwhile collected the blood pumped out from the left ventricle during this time by simply moving the end of the outflow tube S (Plate 7) from the funnel x to a graduated cylinder at the beginning of the 30 seconds, and back again to the funnel at the end. The kymograph was then stopped, the observation numbered upon the roll of the kymograph paper and also in the note-book, and the quantity of blood pumped out, the time of the observation, the venous pressure used during the observation, and the temperature of the blood flowing into the heart as given by the thermometer p, noted down. After the conclusion of an experiment the tracings were carefully examined, and the pulse-rate and the mean arterial pressure during each observation ascertained. After each observation, in place of the blood collected, about an equal amount of warmed blood, a supply of which was kept at hand, was poured back into the receiving flask through the funnel F.

In giving the results of our experiments, it will be convenient to consider them under four different heads, viz.:—

I. The maximum quantity of blood which can be thrown out from the left ventricle at a single systole.

II. The influence of variations of arterial pressure on the work done by the heart.

III. The influence of variations of venous pressure on the work done by the heart.

IV. The influence of variations of pulse-rate on the work done by the heart.

I.

The maximum quantity of blood which can be thrown out from the left ventricle at a single systole.

Our method of working in determining this quantity was as follows:—After the animal had been placed safely in the warm case, and all the connexions had been made, an observation was immediately taken in the way described, at a venous pressure of 10 centims.; the pressure was then raised 5 or 10 centims. and another observation taken, and so on, until a limit was reached, that is, a point beyond which increase of venous pressure did not cause an increased outflow from the aorta. The venous pressure was then brought back to 10 centims., and an observation taken as a control experiment to determine whether or not the condition of the lungs in the meantime had been such as to interfere with the passage of blood to the left auricle.

Below is given a table showing the results of six experiments upon this point; the complete records of these experiments will be found farther on under Section III., with the exception of those of May 9th and May 30th. The control observation in all the experiments, with the exception of the two just named, in which it was not made, showed that the passage through the lungs had not yet become seriously obstructed. This part of the experiment, indeed, was generally completed within a few minutes, and before the lungs had become noticeably œdematous. The temperatures given are those of the blood flowing into the right side of the heart.

The weight of the heart is given together with that of the whole animal, though there does not appear to be any constant relationship between it and the weight of blood pumped out of the ventricle at each systole. In weighing the heart the vessels springing from it were cut off at their origin, superfluous fat removed, and the cavities of the heart cut open and cleaned.

TABLE showing the maximum quantity of blood which can be thrown out from the left ventricle at a single systole.

No. of experiment.	Date. 1882.	Weight of Dog.	Weight of heart.	Temperature of blood flowing into the heart, C.	Heart beats in 30 seconds.	Venous pressure in centims. of blood.	Arterial pressure in millims. of mercury.	Total outflow from the aorta in 30 seconds in cub. centims.	Outflow from the aorta at each systole in cub. centims.
		grms.	grms.	°					
1	April 4	5891	51·5	36	99·5	36·8	109	576	5·79
2	„ 13	8125	92	34·25	86·5	50	135	750	8·67
3	„ „	„	„	35·25	84	58	134	715	8·51
4	„ 18	7725	63	37	103	70	143	850	8·25
5	May 2	8610	76	35·5	89·5	60	138	982	10·97
6	„ 9	5645	73	35	82·5	35	112	490	5·94
7	„ 30	9555	81·5	37	102	59	121	950	9·31

Observations on the preceding table.—In experiment 1, April 4th, it is probable that the limit was not quite reached, as will be seen by referring to the complete record of that experiment (see Section III.); the apparatus at that time being arranged so that 36·8 centims. was the highest venous pressure that could be obtained.

In experiment 4, April 18th, the limit was practically reached at a venous pressure of 60 centims. The right auricle then received all the blood the heart could pump out.

In experiment 7, May 30th, we are not positive that the limit was completely reached, no higher venous pressure than that recorded was tried, on account of the object for which the experiment was performed (see Section IV.). This experiment was introduced into this table, since it had been found in the other experiments that the maximum outflow from the aorta was obtained at or below a venous pressure of 60 centims. Since the Dog in this case was somewhat larger than those usually experimented upon, it is possible that a larger outflow might have been obtained at a higher venous pressure.

The ratio of the weight of blood thrown out at each systole to the weight of the animal is given in the following table. The specific gravity of the defibrinated Calf's blood is taken as 1050; an accurate determination in one case gave 1047.

April 4.	$5·79 \times 1·05 = 6·08 \div 5891 = ·00103$
„ 13.	$8·67 \times 1·05 = 9·10 \div 8125 = ·00112$
„ 18.	$8·25 \times 1·05 = 8·66 \div 7725 = ·00112$
May 2.	$10·97 \times 1·05 = 11·52 \div 8610 = ·00134$
„ 9.	$5·94 \times 1·05 = 6·24 \div 5645 = ·00111$
„ 30.	$9·31 \times 1·05 = 9·78 \div 9555 = ·00102$

The agreement amongst the results is as close as could be expected, when we remember the number of disturbing conditions which may come into play.

One of the most important causes of variation, the value of which we did not fully recognise until our experiments had nearly drawn to a close, is to be found in the pulse-rate; this, as will be shown in Section IV., exercises a marked influence on the amount of blood thrown out at each systole.

Omitting the experiments of April 4th and May 30th, since in both cases the maximum was not quite reached, we find that *the mean ratio of the maximum weight of blood thrown out from the left ventricle at a single systole to the whole body weight is* ·00117 *or* $\frac{1}{855}$, *for a mean pulse-rate of* 180 *per minute.*

Since the slowing influence of the vagi is removed from a heart isolated in this way, the pulse-rate of course is greater than in the normal Dog.

The average pulse-rate in a living Dog may be taken as about 120 per minute. We have as yet only one experiment, that of May 30th (see Section IV.), to show what the maximum outflow at each systole is when the heart is beating at this rate. According to that experiment the ratio of the maximum weight of blood forced out

from the left ventricle at each systole to the weight of the animal, when the heart is beating at 120 per minute, is about ·0014, or $\frac{1}{700}$.

It should be mentioned that care was taken in these experiments that the heart should receive an abundant supply of blood. The possible outflow from the flasks in 30 seconds for each venous pressure used was determined beforehand, and found to exceed by several hundred cubic centimetres the actual quantities pumped out by the heart.

When we come to apply the knowledge obtained in this way from the isolated heart to the heart in the normal animal, we are met with the difficulty of deciding which of the results to take as most nearly representing the actual condition of things in the body. For several reasons we are inclined to believe that the maximum outflow comes closer to the average quantity thrown out during life at each systole than any other we might take; in other words we think it very probable that the left ventricle during life is distended during each diastole to about its maximum capacity. Such a supposition is supported by the work of Roy (4) on the Frog's heart.

Roy found for the Frog that with an intra-ventricular pressure of 15 centims., the capacity of the ventricle had practically reached its limit, and that this is just about the amount of intra-ventricular pressure during life, "The intra-ventricular pressure during diastole, so far as it is governed by the auricles, will vary from 2 to 10 centims., precisely the limit at which the ventricle has its greatest possible distensibility within the limits of elasticity."

Another point which may be brought forward that lends some probability to this view, is found in a consideration of the time required for a complete circulation of the blood to take place. Knowing the proportion of the total weight of blood to the weight of the Dog, and the quantity of blood discharged from the heart at each systole, it is evident that we have a ready means of determining the time necessary for the completion of a circulation. Let us see how the time obtained by supposing that our maximum quantity represents the true capacity of the ventricle during life agrees with the results obtained from Dogs by direct experiment.

Taking a Dog weighing 8000 grms., the total quantity of blood will be equal to $8000 \times \cdot076 = 608$ grms. The weight of blood thrown out from the left ventricle at each systole, with a pulse-rate of 120, will be about $8000 \times \cdot0014 = 11\cdot2$ grms. The number of systoles then that must occur in order for the total weight of blood to make a complete circuit through the left ventricle will be $608 \div 11\cdot2 = 54$; and 54 systoles at the given pulse-rate will take 27 seconds.

Vierordt, in his experiments on Dogs, found that the greatest time required for a salt injected into the jugular vein to be detected in the blood of the femoral vein was 21·76 seconds; his mean result from four experiments was 18·08 seconds.

The number obtained from our calculation is somewhat higher, as in the nature of the case it should be, since Vierordt's experiments were directed to only one of the many paths open to the blood in normal circulation, some of which will require

a longer time to traverse, as for instance, those in which the portal system is included, some a shorter time.

If we take the ratio of the weight of blood pumped out at each systole to the body weight as given by VOLKMANN, and with which that of VIERORDT is almost identical, viz., ·0025, the time necessary for a complete circulation in the hypothetical case above would be about 15 seconds.

The time obtained by such a calculation represents in reality the average time for all the numerous possible paths. Of the various paths open for the blood to take after leaving the heart, those in the course of which only two capillary regions are interposed will practically take about the same time to traverse, the velocity in the arteries and veins being such that mere distance from the heart will add but little to the time required. For that large quantity of blood which, sent out from the left ventricle, returns to it again only after having passed through three capillary regions, the time required for circulation will naturally be greatly increased. Hence the average time for all the different paths should be somewhat greater than the time found necessary by VIERORDT for the jugular-femoral path, as is the case with the time obtained by our calculation; certainly not less, as would follow if VOLKMANN's ratio were correct.

Another consideration which influences us in supposing that the maximum outflow at each systole from the isolated heart is about the normal outflow during life, is based on the pressure in the left auricle.

As far as we know, no one has ever determined the pressure in the left auricle during life without opening the thorax, but it is fair to suppose that it is as great as that in the right auricle. The maximum pressure in the right auricle of the Dog, according to an experiment of GOLTZ and GAULE (5), is about 19·6 millims. of mercury. We determined in one of our isolated hearts the pressure in the left auricle (in a way described in Section III.) for each different venous pressure used on the right side. According to this experiment the mean pressure in the left auricle when the feeding-flask stood at a height of 60 centims. above the right auricle, was only 16 millims. of mercury, the maximum pressure 20 millims., and consequently no greater than that which it is probable exists during life. Our maximum outflow was obtained in all cases either at or below a venous pressure on the right side of 60 centims.

The mean ratio of the weight of blood thrown out at each systole to the body weight, obtained by VOLKMANN for the Dog, is ·0027, or about twice the ratio obtained from our experiments. That there could have been an error of such magnitude in the method employed by us does not seem at all possible, and when we consider, on the one hand, the very uncertain data upon which VOLKMANN's results are based and the complexity of the disturbing conditions, and, on the other hand, the comparative simplicity and directness of the method we have used, its freedom from sources of error, and the agreement of different experiments, we are

justified, we think, in claiming that our results, at least as far as the Dog is concerned, come nearer to the truth than do those of VOLKMANN or of VIERORDT.

Any inference from the results obtained for the Dog to the heart of Man will in the present condition of our knowledge be more or less uncertain. VIERORDT concludes, though upon no very firm grounds, that the weight of blood sent out from the ventricle at each systole in different animals is nearly proportional to the body weight. VOLKMANN also takes the same ratio $\frac{1}{400}$ as holding good for different Mammals.

If the ratio found by us for the Dog can be applied directly to Man it will support the results of FICK's experiments.

There is one fact, however, which it seems to us makes such an inference inadmissible, and that is the difference in pulse-rate between the heart of the Dog and the heart of Man: the average pulse-rate for Man is about 72 per minute, the average pulse-rate for the Dog about 120 per minute. Ought not this to make a difference in the amount of blood thrown out at each systole?

If the supposition is true that the ventricle in the Dog, and presumably in Man also, is distended during each diastole to about its maximum capacity, it would seem that variations in pulse-rate should have but little influence upon the quantity of blood ejected at each systole. From our experiments on the influence of pulse-rate on the outflow from the Dog's heart (see Section IV.), even when a pressure was used that gave at the ordinary temperature at which the blood was kept the maximum outflow, or very nearly the maximum outflow at each beat, it was found that slowing the pulse-rate increases very considerably the outflow at each beat. It is true that this may have been owing to the fact that the method used for slowing the pulse-rate, viz., by running cold blood through the heart, may have caused more or less change in the elastic properties of the ventricular walls. The whole question is one that rests as yet, as far as our experiments are concerned at least, upon suppositions that lack experimental confirmation. We hope ultimately, after carrying out similar experiments upon other animals, to be in a better condition to speak on the subject.

II.

Influence of variations of arterial pressure upon the work done by the heart.

In the experiments made upon this point the venous pressure was kept constant at 15 or 20 centims. of defibrinated Calf's blood (11·7 to 15·6 millims. of mercury); the arterial pressure was varied by simply raising or lowering the end S of the outflow tube t, (Plate 7). That variations of arterial pressure have no direct effect on the pulse-rate of the isolated Dog's heart has been clearly proved by Professor MARTIN's experiments. It would have been preferable, perhaps, to have kept the venous

pressure at the height at which the maximum outflow from the left ventricle was obtained, since in this case we believe that the left ventricle works under conditions most closely resembling those to which it is subject during life; but owing to the rapidity with which our flasks were emptied at these high pressures, and other mechanical difficulties, this was not attempted.

The heart was allowed to work for a short time, from one to two minutes, at each given arterial pressure before an observation was made.

We give below two examples of the results obtained; several other experiments were made, but the two given were those in which the heart and lungs were in the best condition, and the pulse-rate remained very nearly constant.

The work done in gramme-meters at each systole of the left ventricle at various arterial pressures is given in the last column, and was calculated by multiplying the amount of blood thrown out at each systole into the height to which it was raised, making of course the necessary corrections for the specific gravity of the blood used. The formula which we employed is $W = A.s.\frac{H}{1000} \cdot \frac{S}{s} = \frac{A.H.S.}{1000}$, in which W represents the work done, A the quantity in cubic centimetres thrown out from the ventricle at each systole, H the arterial pressure in millimetres of mercury, S the specific gravity of mercury, and s the specific gravity of the blood.

The arterial pressure was measured in the carotid, and is no doubt a little less than that at the root of the aorta.

In both the experiments given the observations upon arterial pressure were made after a series of observations at different venous pressures had been taken, the results of which are given in detail in Section III. under the same dates.

TABLE showing the effect of variations of arterial pressure on the work done by the heart.

April 13, 1882.—Weight of Dog, 8125 grms. Weight of heart, 92 grms.

Observations.	Time, P.M.	Temp. C. in superior cava.	Beats in 30 seconds.	Arterial pressure in carotid. Millims. of mercury.	Venous pressure in superior cava. Centims. of blood.	Outflow in 30 seconds. Cub. centims.	Outflow in 1 beat. Cub. centims.	Work done at each systole of the left ventricle in gramme-metres.
	h. m.	°						
1	2 14	35·75	83·5	112	20	375	4·49	6·78
2	2 16	35·25	78·5	88	20	360	4·58	5·45
3	2 19	36+	80	62	20	379	4·74	3·97
4	2 21	36+	81·5	92	20	367	4·50	5·59
5	2 24	36+	82	120	20	367	4·48	7·25
6	2 26	36·5	82	142	20	355	4·33	8·30
7	2 28	36·5	82	108	20	357	4·35	6·34

May 2, 1882.—Weight of Dog, 8610 grms. Weight of heart, 76 grms.

Observations.	Time, P.M.	Temp. C. in superior cava.	Beats in 30 seconds.	Arterial pressure in carotid. Millims. of mercury.	Venous pressure in superior cava. Centims. of blood.	Outflow in 30 seconds. Cub. centims.	Outflow in 1 beat. Cub. centims.	Work done at each systole of the left ventricle in gramme-metres.
	h. m.	°						
1	3 46	34·5	82	120	20	385	4·69	7·59
2	3 48	35·25	83	84	20	375	4·52	5·13
3	3 49	35+	83·5	58	20	360	4·31	3·40
4	3 51	34·5	82	107	20	372	4·54	6·56
5	3 53	35	79·5	138	20	345	4·34	8·09
6	3 55	35	82	147	20	365	4·45	8·82
7	3 56	35−	81·5	136	20	361	4·43	8·13
8	3 57	34·75	81·5	62	20	350	4·29	3·59

It is seen from the tables that *variations of arterial pressure from* 58 *to* 147 *millims. of mercury have practically no effect whatever on the quantity of blood sent out from the ventricle at each systole.* The small differences that appear easily come within the limits of error. The methods of catching the blood is one that will unavoidably introduce small errors. Another source of error is connected apparently with the use of Calf's blood. After the heart had been working in the case for some time, it was almost always found that the pericardium was tightly filled with exuded serum, preventing complete distension of the ventricle during diastole, and consequently diminishing the outflow—in such cases by cutting a slit in the pericardium the outflow would immediately increase.

The observations given in the table were all taken before this filling of the pericardium had become sufficiently advanced to cause any important error; in later observations in the course of the same experiments its influence was very marked. The figures as they stand, however, show clearly, as we have said, that, within the limits given, variations of arterial pressure have no direct effect on the amount of blood thrown out from the left ventricle. For how much wider limits than those indicated this statement may be true, we cannot yet say. It is also clear that, as Professor MARTIN had already proved (10), the pulse-rate remains unchanged. Since now the work done by the contraction of the ventricle depends on two factors, viz., the amount pumped out at each systole, and the height to which this amount is raised, and one of these factors remains practically constant, it follows that *the work done by the left ventricle of the Dog's heart varies directly as the arterial pressure against which it works within the limits named above.*

BLASIUS (6), in his experiments on the isolated Frog's heart, found that the work of each single beat increased for a time with increase in arterial pressure, but that, nevertheless, "die Intensität des Wachsthums mit nur wenigen Ausnahmen allmählich abnimmt."

By the investigations of WEBER, HEIDENHAIN, FICK, and others, it has been proved for ordinary skeletal muscles that the work done in contracting, measured by the product of the load into the lift, increases up to a certain limit with the load to be raised. The increase in work, however, is not proportional to the increase of load, since as a general rule the lift is diminished as the load is increased, except, perhaps, for minimal weights. If, now, aortic pressure is taken as the equivalent of the load which an ordinary muscle raises when it contracts, the law given above for the work of the left ventricle may be expressed in the terms of muscle physiology in this way. The work done by the heart muscle when it contracts, measured by the product of the weight of blood ejected at each contraction into the height of aortic pressure, not only increases with the load against which it contracts, but increases in direct proportion to the load, within the limits given. It is not probable that this proportional increase of work by the heart muscle is owing to any nervous mechanism co-ordinating the discharge of energy with the resistance to be overcome. Considering it as a muscle phenomenon alone, two explanations suggest themselves. It might be conceived that within the limits given, the total energy liberated at each contraction remains constant, and that that portion of it which is not used up in external work disappears as heat liberated in the heart itself. So that as the arterial pressure increases, making the resistance to be overcome greater, a correspondingly greater portion of the energy appears as external work, and *vice versâ*. Outside of the waste of energy which such a supposition involves, the study of the development of heat in a contracting skeletal muscle teaches us that for it, at least, there is no such inverse proportion between the amount of heat liberated and of external work done in a muscle contracting under different loads. The curves of heat development and of mechanical work, on the contrary, follow a somewhat similar course. An explanation more in accordance with what is known of the physiology of ordinary muscle is found in the supposition that as the load increases a greater amount of energy is liberated, in consequence of some change in the molecular state of the ventricular muscle associated with increased tension at the commencement and during the early stages of its contraction. This is the supposition adopted for ordinary muscle; as FOSTER states it, "the tension of the muscular fibre increases the facility with which the explosive changes resulting in a contraction take place" (Physiol., 1883, p. 88). The difference between the two muscles is that for the heart muscle the energy liberated as external work bears a direct proportion to the tension exerted by the load, while for ordinary muscle this is not true. The lift of an ordinary muscle when contracting is represented, in the case of the heart muscle, by the extent of the contraction, measured by the volume of blood ejected. Since within the range of arterial pressures given the volume of blood thrown out at each systole remains the same, it follows that the extent of the contraction is unchanged. The most probable interpretation of this fact is that the contraction in each case is maximal, and completely empties the ventricular cavity; a conclusion which is in accordance with the work of BOWDITCH, KRONECKER, and others on the isolated Frog's heart.

A curve of work constructed upon the arterial pressures as abscissas, and the work done at each beat of the ventricle under these pressures as ordinates, would, within the limits for which we have investigated it, be a straight line. Owing to the sources of error which we have enumerated above, the results were not sufficiently accurate to construct such a curve.

III.

Influence of venous pressure on the work done by the heart.

In our experiments on the maximum outflow from the ventricles at each systole the venous pressure was varied, as stated, from 10 centims. to 60 or 70 centims. The complete tables of four of the experiments are given below.

In accordance with the results of Professor MARTIN'S previous work, it was found that variations of venous pressure from 10 centims. to even as high as 70 centims. have no direct effect on the pulse-rate.

It was not possible to keep the arterial pressure constant, since at the higher venous pressures the left ventricle pumped out much more blood at each systole, and the increased outflow caused an increased tension in the outflow tubes and the roots of the great arteries still connected with the left ventricle. Since, however, as we have seen, the amount of outflow is not affected by the arterial pressure within the limits occurring in the experiments, we have sought to eliminate the influence of the variations in arterial pressure on the work done, by calculating the work for 100 millims. arterial pressure in all cases, and placing the results in the column to the right of those calculated from the arterial pressures recorded; in this way a clearer idea of the influence of venous pressure alone on the work done by the heart is obtained—the same thing is shown, of course, in the column giving the outflows at each beat.

TABLE showing the effect of variations of venous pressure on the work done by the heart.

April 4, 1882.—Weight of Dog, 5891 grms. Weight of heart, 51·5 grms.

Observations.	Time.	Temp. C. in superior cava.	Beats in 30 seconds.	Arterial pressure in carotid. Millims. of mercury.	Venous pressure in superior cava. Centims. of blood.	Outflow in 30 seconds. Cub. centims.	Outflow in 1 beat. Cub. centims.	Work done at each systole of the left ventricle, in gramme metres.	
								With arterial pressure actually observed.	With arterial pressure = 100 millims.
	h. m.	°							
1	2 56	38	116·5	88	10	255	2·19	2·60	2·96
2	2 58	38+	120	92	15	333	2·77	3·44	3·74
3	2 59	38	120	96	20	404	3·37	4·37	4·55
4	3 00	38+	120	100	25	489	4·08	5·50	5 50
5	3 01	38	116	106	30	582	5·02	7·17	6·78
6	3 03	37	116	110	36·8	629	5·42	8·04	7·32
7	3 06	..	113	107	35	610	5·40	7·80	7·29
8	3 09	36·5	106	88	10	230	2·17	2·58	2·93
9	3 11	36·5	105·5	92	15	299	2·83	3·51	3·82
10	3 12	36	104	100	20	381	3·66	4·93	4·94
11	3 13	36	103·5	100	25	460	4·44	5·99	5·99
12	3 15	36	101·5	102	30	506	4·99	6·87	6·74
13	3 16	36—	101·5	107	35	572	5·63	8·13	7·60
14	3 17	36—	99·5	109	36·8	576	5·79	8·52	7 82
15	3 20	35·5	99·75	88	10	175	1·75	2·08	2·36

April 13, 1882.—Weight of Dog, 8125 grms. Weight of heart, 92 grms.

Observations.	Time.	Temp. C. in superior cava.	Beats in 30 seconds.	Arterial pressure in carotid. Millims. of mercury.	Venous pressure in superior cava. Centims. of blood.	Outflow in 30 seconds. Cub. centims.	Outflow in 1 beat. Cub. centims.	Work done at each systole of the left ventricle, in gramme-metres.	
								With arterial pressure actually observed.	With arterial pressure = 100 millims.
	h. m.	°							
1	1 40	36—	94·5	105	10	220	2·33	3·30	3·15
2	1 41	36—	89	112	20	400	4·49	6·78	6·06
3	1 43	36	92	121	30	535	5·81	9·48	7·84
4	1 44	36—	92	125	35	618	6·71	11·30	9·06
5	..	34·5	89·5	129	40	680	7·59	13·21	10·25
6	..	34·5	89·5	131	45	690	7·71	13·63	10·41
7	..	34·25	86·5	135	50	750	8·67	15·79	11·70
8	..	35·75	93	131·5	58	700	7·53	13·35	10·17
9	..	35—	93	105	10	202	2·17	3·08	2·93

New series: on same animal.

Observations.	Time.	Temp. C. in superior cava.	Beats in 30 seconds.	Arterial pressure in carotid. Millims. of mercury.	Venous pressure in superior cava. Centims. of blood.	Outflow in 30 seconds. Cub. centims.	Outflow in 1 beat. Cub. centims.	Work done at each systole of the left ventricle, in gramme-metres. With arterial pressure actually observed.	With arterial pressure = 100 millims.
	h. m.	°							
10	1 57	35	87·5	105	10	220	2·51	3·55	3·39
11	1 58	35	88·25	113	20	375	4·25	6·48	5·74
12	2 00	34·5	88	120	30	510	5·79	9·36	7·82
13	2 03	35–	88	126·5	35 (?)	605	6·88	11·74	9·29
14	2 07	35	85	132·5	50	705	8·29	14·81	11·19
15	2 10	35·25	84	134	58	715	8·51	15·40	11·49

April 18, 1882.—Weight of Dog, 7725 grms. Weight of heart, 63 grms.

Observations.	Time.	Temp. C. in superior cava.	Beats in 30 seconds.	Arterial pressure in carotid. Millims. of mercury.	Venous pressure in superior cava. Centims. of blood.	Outflow in 30 seconds. Cub. centims.	Outflow in 1 beat. Cub. centims.	Work done at each systole of the left ventricle, in gramme-metres. With arterial pressure actually observed.	With arterial pressure = 100 millims.
	h. m.	°							
1	2 18	37·5	103	99	10	204	1·98	2·65	2·67
2	2 19	37+	97·5	106	20	390	4·00	5·72	5·40
3	2 21	36	95	116	30	545	5·74	8·99	7·75
4	2 23	36·25	98·5	126	40	667	6·77	11·51	9·14
5	2 25	36–	97·5	131	45	720	7·38	13·05	9·96
6	2 27	37–	103	133	50	755	7·33	13·16	9·90
7	2 29	36+	102·5	136	55	781	7·62	13·98	10·29
8	2 32	36+	103	143	60	841	8·16	15·75	11·02
9	2 34	36	103·5	142	65	850	8·21	15·73	11·08
10	2 38	37	103	143	70	850	8·25	15·91	11·14
11	2 41	36·5	99	99	10	150	1·51	2·01	2·04

May 2, 1882.—Weight of Dog, 8610 grms. Weight of heart, 76 grms.

Observations.	Time.	Temp. C. in superior cava.	Beats in 30 seconds.	Arterial pressure in carotid. Millims. of mercury.	Venous pressure in superior cava. Centims. of blood.	Outflow in 30 seconds. Cub. centims.	Outflow in 1 beat. Cub. centims.	Work done at each systole of the left ventricle, in gramme-metres.	
								With arterial pressure actually observed.	With arterial pressure = 100 millims.
	h. m.								
1	3 19	37°·75	95·5	113	10	240	2·51	3·82	3·39
2	3 21	37	93	121	20	473	5·08	8·29	6·86
3	3 23	37·5	96	126	30	617	6·42	10·91	8·67
4	3 27	37−	93·5	134	40	780	8·34	15·08	11·26
5	3 30	36+	91·5	135	50	861	9·40	17·12	12·69
6	3 33	35·5	89·5	138	60	982	10·97	20·43	14·81
7	3 36	36−	87	140	65	940	10·80	20·40	14·58
8	3 40	35+	87	140	70	940	10·80	20·40	14·58
9	3 43	35	84	112	10	200	2·38	3·60	3·21

The great effect which increase of venous pressure and the attendant increase in the blood-flow have upon the total outflow from the left side of the heart, is shown in a striking manner by the preceding tables. From the numbers in the last column it is seen that *the work done by the left ventricle at each systole increases with the venous pressure, but not proportionally, up to the point of maximum work.*

One must be certain in such experiments that at each venous pressure used the quantity of blood sent into the heart is greater than that which is pumped out; in all cases the possible quantity of blood which could flow into the right side of the heart from the flasks at the different pressures was determined beforehand, and found to exceed the actual quantities thrown out from the left side in any given time.

The maximum pressure in the right auricle of the Dog during life is, according to GOLTZ and GAULE, 19·6 millims. of mercury. The pressure to which the right auricle was exposed in our experiments before the maximum outflow was obtained, varied from 27·2 millims. to about 46 millims. of mercury. Such pressures place the right side of the heart under conditions different from those which exist during life. However the right side of the heart was affected by these high pressures, the left side, with which we are more immediately concerned was, as will be shown below, under pressures which in all probability kept within the limits of pressures to which it is exposed during life.

It is certain that the most direct factor influencing the quantity of blood sent out from the ventricle, and hence the work done by the ventricle, is the intra-ventricular pressure by which the ventricle is distended during diastole. Leaving out the aspiratory action of the thorax, the intra-ventricular pressure during life must be mainly owing to the action of the auricle, since the pressure in the great veins

emptying into the auricle probably never rises to any important positive value; indeed, according to the experiments of LUDWIG, VOLKMANN, WEYRICH, and others, has always a mean negative value. The contraction of the auricles, then, must have the most important and direct effect upon the work done by the ventricles, and we are able to confirm for the Mammalian heart the statement made by ROY (8) for the Frog's heart, viz., "The work of the heart in the living animal is governed chiefly by the auricles, the ventricle influencing the amount of work done only indirectly."

In calculating the work done by the left ventricle, we have made no allowance for the venous pressure by which the left ventricle was distended.

A part only, though the much greater part, of the work done at each beat of the ventricle, as given in the tables, is owing to the active contraction of the ventricle itself, the other part is proportional to the pressure by which the ventricle is distended, and is owing to the elastic reaction of its walls.

With a desire to learn how great a correction must be made for this factor, as well as to find out the maximum pressure in the left auricle with the highest venous pressure used, we endeavoured to use upon our hearts the device employed by WALLER (9) upon Rabbits for ascertaining pressure in the left auricle.

After the heart was in the warm chamber and going well, the pericardium was slit open, the tip of the left auricular appendage seized with a pair of forceps, and gently pulled into view; the appendage was then clamped lower down with a weak clamp made especially for the purpose, a slit cut in its walls, and a cannula filled with salt solution 0·6 per cent. and connected by a piece of lead tubing, also filled with 0·6 per cent. salt solution, with a mercury manometer, was introduced into its cavity and firmly tied; the clamp was then removed.

Of three such experiments tried, two failed, the third was so far successful that the results obtained from it can be accepted as approximately correct. The beats of the auricle were plainly recorded upon the kymograph paper.

The outflow from the left ventricle at each venous pressure was estimated in the usual way, and was about equal to that obtained from Dogs of the same size in the experiments which have been given.

The results obtained are given in the following table.

June 2, 1882.—Weight of Dog, 6085 grms.

Observations.	Venous pressure in right auricle.			Pressure in left auricle in millims. of mercury.	
	Centims. of blood.		Millims. of mercury	Mean.	Max.
1	10	=	7·8	8	..
2	20	=	15·6	10	..
3	30	=	23·3	12	..
4	40	=	31·1	13·5	15·5
5	50	=	38·9	15	19
6	60	=	46·7	16	20
7	50	=	38·9	15	20
8	40	=	31·1	14	18
9	30	=	23·3	13	16
10	20	=	15·6	10	12·5
11	10	=	7·8	8	10

It is seen that the mean intra-auricular pressure of the left heart at the highest venous pressure used was only 16 millims. of mercury, which, as we have before said, is probably inside the limits which auricular pressure may reach during life, that is, if the left auricle is exposed to as great a pressure as the right, and there is no reason for supposing that it is not. We did not think it necessary to apply the corrections to the tables given of the effect of venous pressure upon the work done by the left ventricle, since except for the purpose of constructing a curve of work the absolute value of the work done by the contracting ventricle is of no especial importance.

IV.

Influence of rate of beat on the work done by the heart.

In endeavouring to arrive at a conclusion as to the average quantity of blood thrown out from the ventricle of Man's heart at each systole upon the basis of the results obtained from the Dog, we were led, as has been said, to consider the influence of pulse-rate upon this quantity.

Looking over the literature of the subject as far as it has been accessible to us, we find that no definite knowledge has been gained upon this point. VOLKMANN, in discussing the effect of changes of pulse-rate upon the mean velocity, says that he can make no definite statement of the relations between the two. By bleeding his animals he got a diminished velocity together with an increased pulse-rate, but it is evident that from such a method of operating no causal relation can be assumed to exist between these two factors.

By cutting the vagi and thus producing a much more rapid pulse, he found that in some

cases this increased pulse-rate was accompanied by a greater velocity, in other cases by a smaller velocity of the blood stream.

VIERORDT found with reference to the relation between pulse-rate and what he calls the "greatness of the systole," *i.e.*, the quantity of blood thrown out at each systole, that sometimes, perhaps in most cases, a diminished pulse was accompanied by an increase in the greatness of the systole, while on the other hand cases were observed in which the reverse happened. The relative greatness of the systole was determined from the number of beats which occurred in the time necessary for the completion of a circulation.

In our experiments we increased or diminished the pulse-rate by raising or lowering the temperature of the blood flowing into the heart, using for this purpose the same method as that described by Professor MARTIN (Phil. Trans., 1883, p. 663).

We give below the records of two experiments.

In the experiment of May 18 a low venous pressure, 20 centims., was used, and besides the thermometer in the inflow tube, another was placed in the left subclavian artery, the bulb projecting into the aorta. The temperatures were read from both of these thermometers at the end of each observation; in the table the temperature on the arterial side is marked A, that on the venous side V. After observation 18 of this experiment, one of the supply flasks unfortunately ran completely empty, allowing some air to get into the heart, so that the succeeding observations could not be trusted. In the experiment of May 30 a venous pressure was used of such a height that, judging from our other experiments, the maximum outflow at each systole for the given pulse-rate was obtained.

In this case a thermometer was not placed in the subclavian artery, since it would have interfered to some extent with the flow from the left ventricle, and owing to the rapidity with which the flasks were emptied, we were not always able to get the temperature of the inflowing blood, nor the times of the observations; these latter however were made at intervals of from one to three minutes.

TABLE showing the influence of the rate of beat on the work done by the heart.

May 18, 1882.—Weight of Dog, 7005 grms. Weight of heart, 59·5 grms.
Thermometer in the inflow tube and in the left subclavian artery.

Observations.	Time.	Temp. C.	Beats in 30 seconds.	Arterial pressure. Millims. of mercury.	Venous pressure. Centims. of blood.	Outflow in 30 seconds. Cub. centims.	Outflow in 1 beat. Cub. centims.
	h. m.	°					
1	1 30	A. 38 + / V. 38 +	114	100	20	325	2·85
2	1 32	A. 38·25 / V. 38·25	113·5	100	20	315	2·78
3	1 36	A. 36 + / V. 36 −	101	100	20	283	2·80
4	1 39	A. 34 + / V. 34 −	90·5	100	20	275	3·04
5	1 42	A. 33 / V. 32·25	79	98	20	260	3·29
6	1 44	A. 31·75 / V. 31 −	70	98	20	250	3·57
7	1 46	A. 31 + / V. 30	66·5	97	20	240	3·61
8	1 47	A. 30·5 / V. 29·75	62·25	97	20	220	3·53
9	1 48	A. 30·25 / V. 29·75	60·5	97	20	208	3·44
10	1 51	A. 29·5 / V. 27·75	55·75	96	20	208	3·73
11	1 52	A. 28·5 / V. 27·5	49·5	96	20	200	4·04
12	1 54	A. 28·5 / V. 27·5	49·75	96	20	193	3·88
13	1 57	A. 27·75 / V. 27	43·5	94 (?)	20	185	4·25
14	1 59	A. 26·5 / V. 25 −	38·5	90 (?)	20	180	4·68
15	2 02	A. 28 / V. 28·5	44	95	20	184	4·18
16	2 04	A. 28·75 / V. 29	47	96	20	192	4·09
17	2 07	A. 31·75 / V. 33	64·5	96	20	230	3·56
18	2 08	A. 32·5 / V. 33·5	70·75	97	20	255	3·60

May 30, 1882.—Weight of Dog, 9555 grms. Weight of heart, 81·5 grms.
Thermometer in the inflow tube.

Observations.	Temp. C.	Beats in 30 seconds.	Arterial pressure. Millims. of mercury.	Venous pressure. Centims. of blood.	Outflow in 30 seconds. Cub. centims.	Outflow in 1 beat. Cub. centims.
1	37°	98	121	59	905	9·23
2	37−	102	124	59	950	9·31
3	34·25	88	123	59	875	9·94
4	34−	80·5	122	59	830	10·31
5	30+	65	123·5	59	780	12·00
6	..	49·5	121	59	670	13·53
7	..	45·75	122	59	670	14·64
8	26·25	35·75	116·5	59	583	16·30
9	..	32·75	116·5	59	525	16·03
10	..	36·5	116·5	59	590	16·16
11	..	46	118	59	643	13·98
12	..	56·25	119	59	663	11·79
13	35−	68	120·5	59	710	10·44
14	37	78·5	120	59	730	9·30

From a consideration of these tables there can be no doubt of the general fact that *a diminution of pulse-rate, brought about by lowering the temperature of the blood flowing into the heart, causes an increase in the quantity of blood thrown out from the ventricle at each systole, and consequently an increase in the work done at each systole; and vice versâ.*

The changes in the outflow from the ventricle at each systole are not, however, inversely proportional to the changes in the pulse-rate, so that the total outflow, and, therefore, the total work during any given period of time, decreases with a diminished pulse-rate, and increases with an increased pulse-rate.

Whether any definite relation, beyond the general one given above, can be established between the pulse-rate and the outflow at each systole, we are not as yet prepared to say; a consideration of this and of some other interesting points which suggest themselves in this connexion must be left for a future paper.

In conclusion, we desire to express our most earnest thanks to Professor MARTIN for the aid and encouragement which he has given us during the progress of this work. We are indebted to him not only for many valuable suggestions in the earlier part of the investigation, when success seemed doubtful, but also for personal assistance which he has sometimes kindly given. The Plate representing the apparatus employed is that which was published with his paper, and it is here reproduced for the convenience of the reader.

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Fig 2

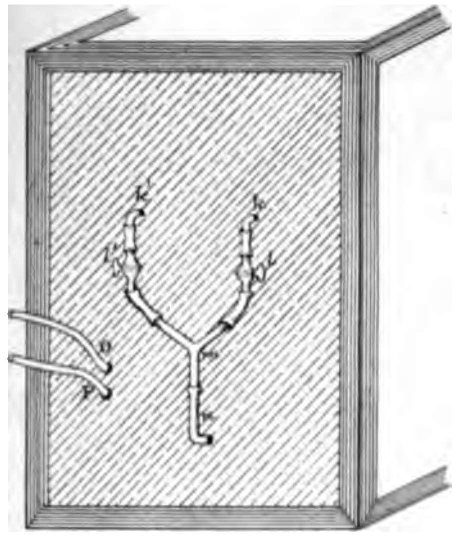
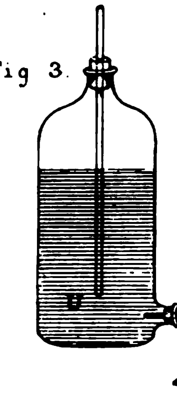
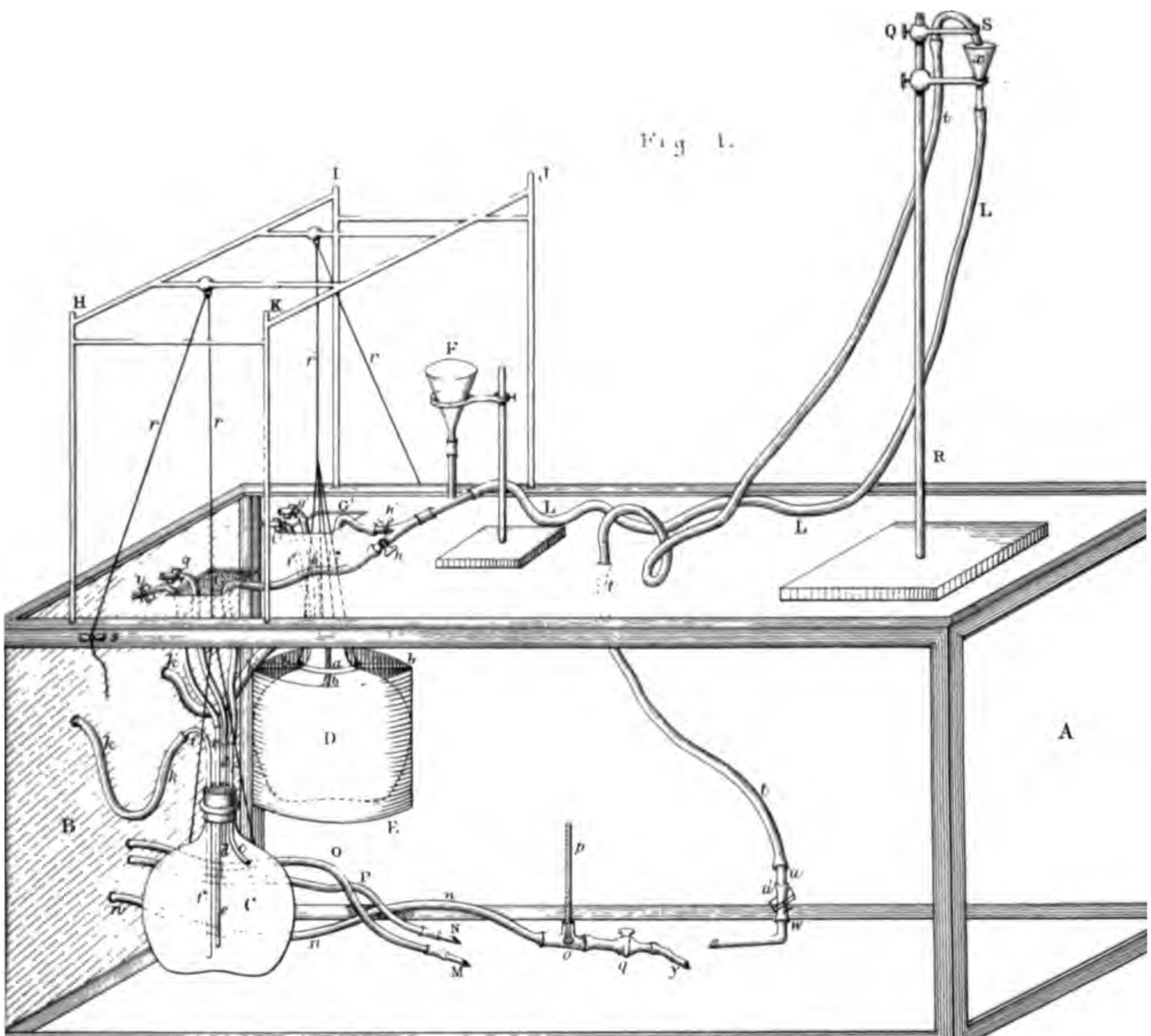


Fig 3.



Fig

Fig 1.



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